EXHIBIT 40

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Patient Warming Excess Heat: The Effects on Orthopedic Operating Room Ventilation Performance

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BACKGROUND: Patient warming has become a standard of care for the prevention of unintentional hypothermia based on benefits established in general surgery. However, these benefits may not fully translate to contamination-sensitive surgery (i.e., implants), because patient warming devices release excess heat that may disrupt the intended ceiling-to-floor ventilation airflows and expose the surgical site to added contamination. Therefore, we studied the effects of 2 popular patient warming technologies, forced air and conductive fabric, versus control conditions on ventilation performance in an orthopedic operating room with a mannequin draped for total knee replacement.

METHODS: Ventilation performance was assessed by releasing neutrally buoyant detergent bubbles ("bubbles") into the nonsterile region under the head-side of the anesthesia drape. We then tracked whether the excess heat from upper body patient warming mobilized the "bubbles" into the surgical site. Formally, a randomized replicated design assessed the effect of device (forced air, conductive fabric, control) and anesthesia drape height (low-drape, high-drape) on the number of bubbles photographed over the surgical site.

RESULTS: The direct mass-flow exhaust from forced air warming generated hot air convection currents that mobilized bubbles over the anesthesia drape and into the surgical site, resulting in a significant increase in bubble counts for the factor of patient warming device ($P < 0.001$). Forced air had an average count of 132.5 versus 0.48 for conductive fabric ($P = 0.003$) and 0.01 for control conditions ($P = 0.008$) across both drape heights. Differences in average bubble counts across both drape heights were insignificant between conductive fabric and control conditions ($P = 0.87$). The factor of drape height had no significant effect ($P = 0.94$) on bubble counts.

CONCLUSIONS: Excess heat from forced air warming resulted in the disruption of ventilation airflows over the surgical site, whereas conductive patient warming devices had no noticeable effect on ventilation airflows. These findings warrant future research into the effects of forced air warming excess heat on clinical outcomes during contamination-sensitive surgery. (Anesth Analg 2013;117:406–11)

Operating room (OR) ventilation has been recognized, historically, as an important component of a multifaceted infection reduction strategy in orthopedics. Starting with the work of Sir John Charnley in the 1960s,[1] 20 years of research established the benefits of using sophisticated ventilation systems to create localized zones of highly filtered air over the surgical site. Clinically, these systems were shown to reduce surgical site microbial exposure[2] and led to the United Kingdom commissioning the first and only randomized clinical trial, which demonstrated a significant reduction in orthopedic infection rates.[3] Recently, though, a number of national studies have shown no infection reduction benefits.[4–6] These results question the value of sophisticated ventilation systems. Although the cause for such failures is presently unknown, changes have been made to OR equipment that may affect ventilation performance; notable among them the introduction of forced air patient warming in the 1990s.

Patient warming is a recognized and necessary standard of surgical care, with warmed patients having better outcomes through reduced blood loss, improved wound healing, reduced duration of hospital stay, improved survival, and reduced surgical site infection rates for "dirty" (colorectal) surgery.[7,8] However, patient warming systems incidentally release excess heat that is not absorbed by the patient. This excess heat naturally rises and may disrupt the intended ceiling-to-floor OR ventilation airflows. Thus, potential for ventilation disruption may be proportional (among many other factors) to the amount of excess heat emitted, which depends on the choice of patient warming technology.[9]

Two general classes of patient warming technology are used intraoperatively. The first, forced air, warms by distributing heated air (up to 43°C) under the surgical

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drapes and over the patient in a large envelope.[10] The second, conductive blankets, uses a resistive heating element or hot water jacket (for heated water blankets) to directly apply heat to the patient's skin.[11] Because conductive blankets are localized in their application, they tend to have higher thermal efficiencies and contribute less excess heat to the environment than forced air.[12] Therefore, in this study, we chose to evaluate the effects of both patient warming technologies versus control (no warming) on ventilation performance. The study was conducted in a standard orthopedic OR having ceiling-to-floor displacement ventilation with a mannequin draped for total knee replacement having upper body patient warming applied. Changes in ventilation airflow patterns were assessed using neutrally buoyant detergent bubbles.

METHODS

OR Characteristics

Experiments were performed in a downward displacement ventilation OR used for orthopedic surgery at the University of Minnesota Hospital (Minneapolis, MN). Ceiling-to-floor airflows are generated by a 2.43 × 2.43 m continuous grid (100% coverage) of diffuser panels over the OR table, each of which contains a final point-of-use high-efficiency particulate air (HEPA) filter. Supply air is centrally pressurized, prefiltered, and then ducted to the individual ORs. The OR used for these experiments received a supply airflow of 51.5 m^3/min, resulting in 19.7 air changes per hour; minimum requirements for hospital ventilation are 15 air changes per hour.[13] Airflow balance is certified yearly. Surgical lighting was provided by 2 Chromophare D650 Plus overhead lights (Berchtold Corporation, Charleston, SC), which were turned off during experiments. OR temperature was set to 20°C.

Airflow Visualization Procedures

High-intensity lighting was used to illuminate neutrally buoyant detergent bubbles having a 4-mm average diameter (referred to herein as "bubbles"). Bubbles were produced by a generator (Sage Action, Ithaca, NY), which used a helium and air supply. The equipment filters the bubbles using a centrifugal classifier that only allows bubbles of neutral buoyancy to pass; those heavier or lighter are discarded. The bubble generator is specifically designed and validated for the visualization of air currents.[14] For photography, a digital camera (500D; Canon, Surrey, UK) was used, and shutter exposure time was set to 1/4 of a second for time-lapsed photography.

Total Knee Replacement Experimental Setup

A mannequin was laid in the supine position and draped in accordance with the standard draping protocol used by the hospital for knee replacement procedures. A perforated drape was used for the proximal limb, with a sterile stocking for the foot and distal limb (Fig. 1). An anesthesia provider dressed in surgical scrubs stood motionless at the head of the table behind the anesthesia/surgery drape. The anesthesia/surgery drape was either (1) clipped to IV poles and raised 0.75 m above the operating table (high-drape), or (2) clipped to IV poles and raised 0.25 m above the operating table (low-drape). The upper body warming device was introduced under the drape and was (1) a torso forced air blanket (Bair Hugger Model 540; Arizant Healthcare, Eden Prairie, MN), (2) a torso conductive fabric blanket (Hot Dog Model B110; Augustine Temperature Management, Eden Prairie, MN), or (3) no warming device (control). The blankets were powered by standard controllers set to 43°C (forced air, Model 750, Arizant Healthcare; conductive fabric, Model WC02, Augustine Temperature Management) and affixed according to manufacturers' instructions. Bubbles were introduced at the head/neck of the mannequin to track under drape resident air movements in the region where the excess patient warming heat was being released. To ensure a consistent release point and direction for the bubbles exiting the generator, the diffuser cone was laid down on the OR head pad and aimed directly into the drape (perpendicular to the raised drape edge).

Figure 1. Total knee replacement setup showing high anesthesia drape position (A) and low anesthesia drape position (B).

Sampling Procedures

Bubble counts over the surgical site were measured using a sequence of 10 photographs taken at 10-second intervals for each experimental run. A 5-minute period was allowed between randomized experimental runs for conditions to equilibrate; all study data were collected on the same day. The number of bubbles reaching the surgical site was determined by counting the number of bubbles intersecting a vertical light curtain in a 0.75 × 0.75 m

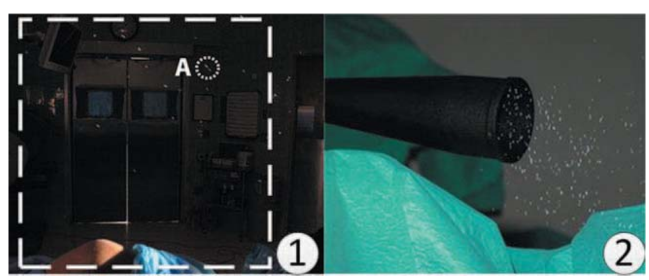

Figure 2. 1, Definition of count region above the surgical site (dashed lines) showing neutrally buoyant detergent "bubbles," which appear as white dots (A) when they intersect the vertical light plane. Photograph is from the forced air warming and high drape experimental run. 2, View of bubbles exiting the diffuser end in still air (outside the operating room in a laboratory).

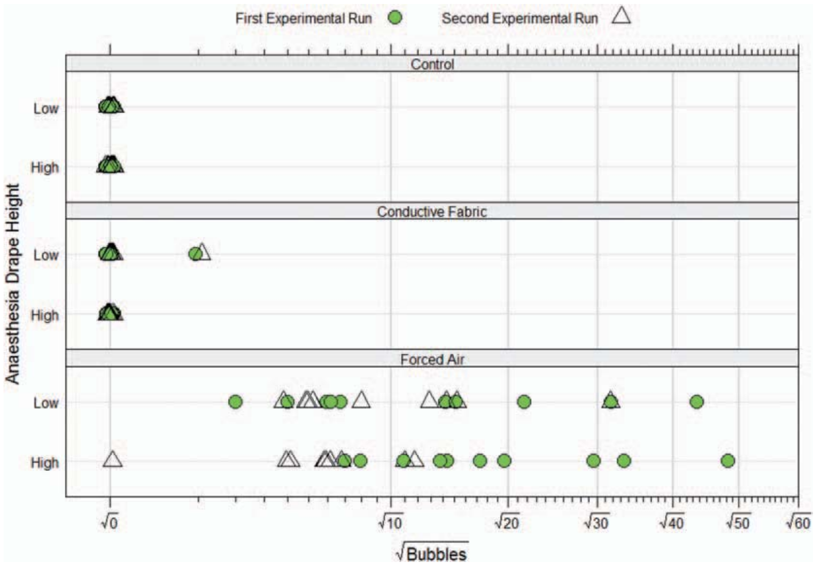

Figure 3. Bubble counts over the surgical site for each photograph (data are jittered to avoid overprinting). Ten photographs were taken for each experimental run.

region directly over the surgical site (Fig. 2). Additionally, time-lapse photography was performed to provide directional information on airflow patterns not captured in bubble count data.

Experimental Design

A replicated (n = 2) $2^1 3^1$ full factorial design was used to assess changes in bubble counts over the surgical site. The experimental factors considered were (1) anesthesia screen (low-drape or high-drape), and (2) patient warming device (conductive fabric, forced air, or no warming device) (control).

Statistical Analysis

A Poisson regression model for overdispersed data was fit having the sum of bubble counts for each experimental run (10 pictures) as the response and the factors identified in the experimental design as predictors plus an interaction term. A log-likelihood ratio test was used to determine the significance of the interaction term by comparing the full model versus an additive model with adjustment for overdispersion; if the interaction term was insignificant, a second set of tests for each additive parameter was performed using a log-likelihood ratio test comparing the parameter deleted additive model versus the full additive model with adjustment for overdispersion. Reported means and standard errors were computed using maximum likelihood parameter estimates and contrasts assuming asymptotic normality (Wald tests). P values correspond to 2-tailed tests and P values <0.05 were considered significant.

RESULTS

Bubble Counts Over the Surgical Site

In viewing the raw bubble count data (Fig. 3), it is apparent that there is a large increase in the number of bubbles reaching the surgical site when forced air warming is in use versus either conductive fabric warming or control conditions. Furthermore, this increase seems to be independent of drape height.

Table 1. Poisson Bubble Count Model Parameters and Their Significance

Model parameter	*P* value
Drape height[a]	0.937
Patient warming device[a]	<0.001
Drape height × patient warming device[b]	0.980

[a] Computed using likelihood ratio deleted parameter tests from the additive model.
[b] Computed using a likelihood ratio comparing full and additive model.

Formal inference using Poisson regression (Table 1) revealed the only significant factor affecting sum of bubble counts to be patient warming device ($P < 0.001$); the factors of drape height ($P = 0.94$) and the interaction term between drape height and patient warming device ($P = 0.98$) were insignificant. With the full additive model (Fig. 4), the use of forced air warming was found to result in a predicted mean sum of bubble counts equal to 132.5 when averaged across both anesthesia drape heights; such a count represents a significant increase in the number of bubbles reaching the surgical site versus both conductive fabric warming ($P = 0.003$) and control conditions ($P = 0.008$), which had predicted mean sum of bubble counts equal to 0.48 and 0.01, respectively. Moreover, differences in the number of bubbles reaching the surgical site were not significantly different between conductive fabric warming and control conditions ($P = 0.87$).

Time-Lapse Photography

With forced air warming, convection current formation was detected in the space between the anesthesiologist's body and the anesthesia drape (Fig. 5). These convection currents were observed to mobilize resident air near the mannequin's head upward and over the topside of the anesthesia drape, which then spilled into the surgical site. Furthermore, the presence of an overhead surgical light had a significant impact on the dynamics of these convection currents; the recirculation zone extending below the light tended to magnify resident air mobilization into the

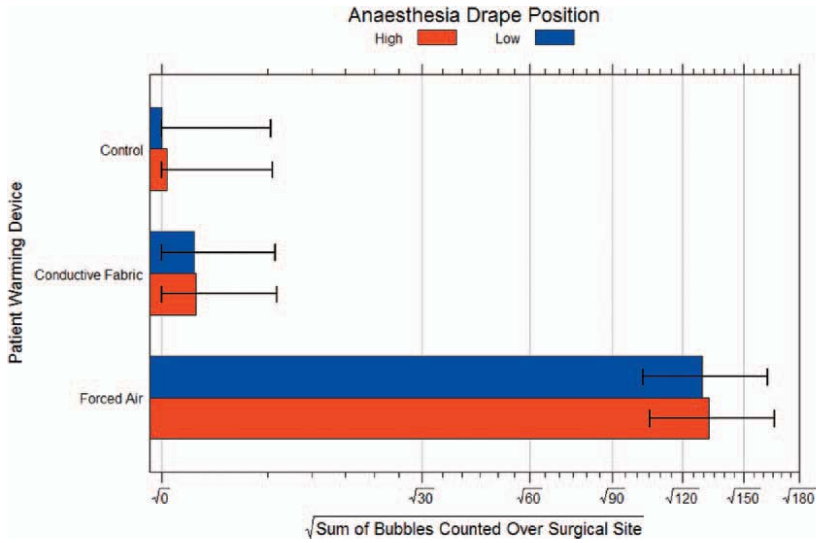

Figure 4. Predicted mean sum of bubble counts (±SEM). Predicted means and standard errors were computed from the full additive model with adjustment for overdispersion.

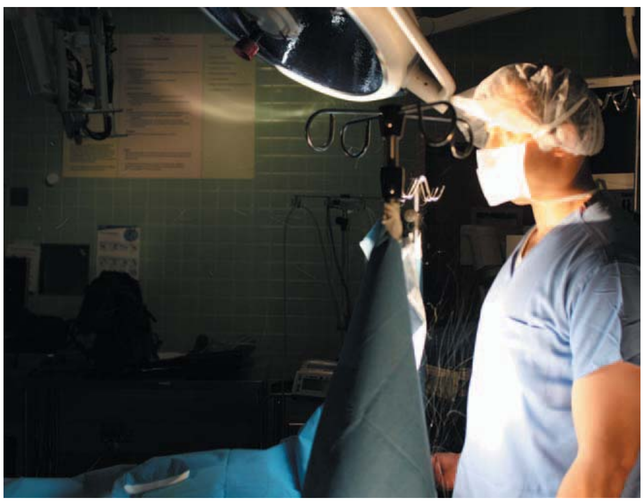

Figure 5. Time-lapse photography of forced air warming showing upward mobilization of neutrally buoyant detergent bubbles caused by hot air convection currents. Note: Bubble diffuser was moved from the experimental position (laid-down on operating room table) to better illustrate the effect for photography.

Figure 6. Time-lapse photography of conductive fabric warming showing no noticeable effect on ceiling-to-floor ventilation airflows (i.e., the neutrally buoyant detergent bubbles are swept down and away from the surgical site). Control conditions looked identical and, thus, are not shown separately. Note: Bubble diffuser was moved from the experimental position (laid-down on operating room table) to better illustrate the effect for photography.

surgical site by redirecting the upward convection currents into the light's "flow-shadow" and over the surgical site. As a note, the surgical lights were not moved over the course of the experiments and their setup is displayed in Figure 1.

In contrast, convection currents were not detected with conductive fabric warming (Fig. 6) and, therefore, there was no apparent upward mobilization of resident air. Instead, ventilation airflows were observed to follow the intended ceiling-to-floor path, sweeping contaminants down and away from the surgical site. Time-lapse photography of control conditions looked identical to those recorded with conductive fabric warming and, as such, are not displayed separately.

DISCUSSION

In this study, we sought to evaluate the effects of patient warming excess heat, using 2 fundamentally different technologies, forced air and conductive fabric, on OR ventilation performance. Under the above-explained experimental conditions, forced air warming was found to have a significant disruptive impact on clean airflow patterns over the surgical site, whereas conductive fabric warming had no noticeable effect versus controls. Moreover, forced air warming was found to establish convection currents that mobilized resident air from nonsterile areas (under the anesthesia drape) upward and into the surgical site. The clinical concern is that convection currents may mobilize under-drape contaminants into the surgical site and/or impede the ventilation systems' ability to clear contaminants from the surgical site. These concerns are most relevant for smaller airborne particles ≤10 μm, such as free-floating bacteria[15] and skin cell fragments,[16] having similar airborne characteristics to the neutrally buoyant detergent bubbles studied (i.e., appreciable suspension times).

The buoyancy-driven convection currents appeared to form in regions of localized ventilation disturbance caused

by surgical lighting, drapes, and personnel. For example, past research has identified surgical lighting to be a significant source of ventilation disruption through the downstream wake and concomitant recirculation zone.[14] In the present study, we were able to visualize this recirculation zone using bubbles and found it to extend approximately 1 m below each light. Such disruption was further magnified by the presence of a raised anesthesia drape, which created a still zone by blocking the natural passage of air out of the ventilation field. Lastly, the presence of an anesthesiologist behind the anesthesia drape added a final flow obstruction[17] and, ultimately, created a channel behind the drape in which ventilation airflows were nearly quiescent. Under these fragile conditions, the mass flow of forced air warming exhaust was sufficiently buoyant to push upward, over the top drape edge, and into the surgical site.

It is worth mentioning, however, that the observed disruption was dependent on our exact setup (i.e., arrangement of draping, lights, and personnel), which did not include the presence of instrument trays and a working surgical team. Thus, we are unsure of the exact degree of ventilation disruption that might occur in a working OR during orthopedic surgery. We can, however, state some observations regarding this extrapolation. First, surgical personnel and their associated movements lead to localized zones of ventilation disruption,[17] a factor that was identified as contributing to the formation of excess heat convection currents in this study. As such, removal of the surgical team from the experimental setup would most likely reduce the incidence of convection current formation. Second, instrument trays act as flow obstructions and would be expected to have a similar effect. Thus, similar ventilation systems, with respect to airflow, diffuser configuration, lighting, and draping arrangement, seem to be at risk for disruption with any surgical team/instrument tray configuration. Third, it should be noted that the head-end surgical light was positioned close to the raised anesthesia drape. This placement was attributable to the height of our surgeon (6 ft., 3 in.), who needed sufficient head room to operate. Thus, for shorter surgeons, different results might be expected. Lastly, it was necessary to turn surgical lights off during the experiment to allow for consistent bubble counts in the intersecting light plane. Given that lighting heat sources tend to adversely affect ventilation performance,[14] our results should be considered conservative.

The most recent articles published on the association between patient warming excess heat and ventilation disruption present contradictory conclusions. Two studies conducted in the United Kingdom have characterized both the thermal basis[9] and airflow patterns[18] supporting the physics behind ventilation disruption in laminar flow ORs. In contrast, a published study in the Netherlands[19] found no evidence of ventilation disruption due to forced air excess heat when evaluated with the DIN 1946:2008-12 standard.[20] This discrepancy in findings is likely related to 2 primary differences in test methods.

First, the surgical lights were positioned in line with the OR table in both of the United Kingdom studies based on common clinical practice, whereas the lights were positioned to the sides of the OR table in the Netherlands study. Second, the United Kingdom study assessing airflow patterns evaluated the effect of patient warming excess heat on interior particle loads, defined as neutrally buoyant bubbles released (1) near the surgeon at floor level, and (2) under the anesthesia drape at the head of the OR table. With the Netherlands study, it is unclear whether the protective effect was assessed for outside particle loads (particles released on the periphery of the ventilation boundary) or inside loads (particles released by the surgeon).

Therefore, it seems that future research is warranted to characterize the clinical conditions under which forced air warming excess heat results in ventilation disruption during surgery. Careful attention should be given to the factors of draping, ventilation airflows, flow obstructions (lighting, instrument trays), and personnel movements, each of which has been identified as affecting this phenomenon. Preferably, this research would be conducted on a national basis covering orthopedic operations in both laminar flow and conventional ventilation environments, including infection-based end points (airborne bacteria, fomites, and/or joint sepsis rates) for an assessment of clinical risk.

DISCLOSURES

Name: Kumar G. Belani, MBBS, MS.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Kumar Belani has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
Conflicts of Interest: Kumar G. Belani received honoraria from NONIN Inc., consulted for NONIN Inc., received research funding from NONIN Inc., received research funding from Augustine Temperature Management, LLC, reported a conflict of interest with Oakstone Publishing, consulted for Cadence Pharmaceuticals, and reported a conflict of interest with Cadence Pharmaceuticals. He is coordinating editor for Oakstone Publishing; he is a speaker for Cadence Pharmaceuticals. His authorship in this article will add to his academic productivity and may have an indirect influence on his compensation from University of Minnesota.
Name: Mark Albrecht, MStat, MBA, BSME.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Mark Albrecht has seen the original study data, reviewed the analysis of the data, approved the final manuscript, and is the author responsible for archiving the study files.
Conflicts of Interest: Mark Albrecht received paid support (salary) from Augustine Temperature Management.
Name: Paul D. McGovern, BSc, MBBS, MRCS, PGCME, FHEA.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the manuscript.
Attestation: Paul McGovern has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
Conflicts of Interest: The author has no conflicts of interests to declare.
Name: Mike Reed, MBBS, MD, FRCS (T&O).
Contribution: This author helped write the manuscript.
Attestation: Mike Reed has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
Conflicts of Interest: The author has no conflicts of interests to declare.

Name: Christopher Nachtsheim, PhD.
Contribution: This author helped analyze the data and write the manuscript.
Attestation: Christopher Nachtsheim has seen the original study data, reviewed the analysis of the data, and approved the final manuscript.
Conflicts of Interest: Christopher Nachtsheim has received consulting fees from Augustine Temperature Management.
This manuscript was handled by: Sorin J. Brull, MD, FCARCSI (Hon).

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